

Amendments to the Claims

This listing of claims will replace all prior versions and listings of claims in the application:

Listing of the Claims:

Claim 1 (currently amended) An antagonist that inhibits angiogenesis by modifying protein-protein interactions, wherein the protein-protein interactions comprise interactions between at least one amino acid sequence within a first protein and at least one amino acid within a second protein, wherein the first protein is a proteolytic enzyme and the second protein is an integrin.

Claim 2 (original) The antagonist of claim 1 wherein the first protein is MMP-9.

Claim 3 (currently amended) The antagonist of claim 1 wherein the ~~first~~ second protein is a β 1-containing integrin.

Claim 4 (original) The antagonist of claim 1 wherein the first protein is MMP-9 and the second protein is a β 1-containing integrin.

Claim 5 (original) The antagonist of claim 4 wherein the protein-protein interactions cause MMP-9 to bind to the β 1-containing integrin.

Claim 6 (original) The antagonist of claim 3 wherein the β 1-containing integrin is α 5 β 1 integrin.

Claim 7 (original) The antagonist of claim 4 wherein the β 1-containing integrin is α 5 β 1 integrin.

Claim 8 (original) The antagonist of claim 1 wherein the protein-protein interactions cause co-localization of the first protein and the second protein on a cell surface or a blood vessel.

Claim 9 (original) The antagonist of claim 1 wherein said antagonist inhibits angiogenesis.

Claim 10 (original) The antagonist of claim 1 wherein said antagonist inhibits tumor growth.

Claim 11 (original) The antagonist of claim 1 wherein said antagonist inhibits metastasis.

Claim 12 (original) The antagonist of claim 1 wherein said antagonist inhibits a disease state.

Claim 13 (original) The antagonist of claim 12 wherein the disease is psoriasis, macular degeneration, a neurological disease, or restenosis in a tissue.

Claim 14 (original) The antagonist of claim 1 wherein said antagonist is a monoclonal antibody.

Claim 15 (original) The antagonist of claim 14 wherein said monoclonal antibody is monoclonal antibody FM155.

Claim 16 (currently amended) The ~~An~~ antagonist of ~~claim 1~~ that inhibits angiogenesis by modifying protein-protein interactions, wherein the protein-protein interactions comprise interactions between at least one amino acid sequence within a first protein and at least one amino acid within a second protein, wherein said antagonist has the binding specificity for at least one target of monoclonal antibody FM155.

Claim 17 (original) The antagonist of claim 1 wherein the antagonist is a polyclonal antibody.

Claim 18 (withdrawn) The antagonist of claim 1 wherein the antagonist is a polypeptide, a linear peptide or a cyclic peptide.

Claim 19 (withdrawn) The antagonist of claim 1 wherein the antagonist is a non-peptidic compound.

Claim 20 (withdrawn) The antagonist of claim 1 wherein the antagonist is a small organic compound.

Claim 21 (withdrawn) The antagonist of claim 1 wherein the antagonist is an oligonucleotide.

Claim 22 (original) The antagonist of claim 1 wherein the antagonist is a humanized or chemically modified monoclonal antibody.

Claim 23 (original) The antagonist of claim 1 wherein the antagonist is a fragment of a monoclonal antibody.

Claim 24 (original) The antagonist of claim 1 wherein the antagonist is conjugated to cytotoxic or cytostatic agents.

Claim 25 (withdrawn) A polypeptide for inhibiting angiogenesis and/or tumor growth wherein the polypeptide specifically binds to MMP-9 with a binding affinity significantly greater than the binding capacity of SEQUENCE ID NO: 3 to MMP-9. ✓

Claim 26 (withdrawn) The polypeptide of claim 25 wherein the polypeptide is a protein

Claim 27 (withdrawn) The polypeptide of claim 25 wherein the polypeptide has a sequence consisting of SEQUENCE ID NO: 1.

Claim 28 (withdrawn) The polypeptide of claim 25 wherein the amino acid sequence of the polypeptide comprises SEQUENCE ID NO: 1.

Claim 29 (withdrawn) The polypeptide of claim 25 wherein the polypeptide is a monoclonal antibody.

Claim 30 (withdrawn) The polypeptide of claim 29 wherein the monoclonal antibody is FM 155.

Claim 31 (withdrawn) A polypeptide for inhibiting angiogenesis or tumor growth wherein the polypeptide specifically binds to a $\beta 1$ containing integrin with a binding affinity significantly greater than the binding affinity of SEQUENCE ID NO: 3 to the $\beta 1$ containing integrin.

Claim 32 (withdrawn) The polypeptide of claim 31 wherein the polypeptide is a protein.

Claim 33 (withdrawn) The polypeptide of claim 31 wherein the polypeptide is SEQUENCE ID NO: 1.

Claim 34 (withdrawn) The polypeptide of claim 31 wherein the amino acid sequence of the polypeptide comprises SEQUENCE ID NO: 1.

Claim 35 (withdrawn) The polypeptide of claim 31 wherein the polypeptide is a monoclonal antibody.

Claim 36 (withdrawn) The polypeptide of claim 35 wherein the monoclonal antibody is FM 155.

Claim 37 (withdrawn) An antagonist that specifically binds with SEQUENCE ID NO: 1 but binds to SEQUENCE ID NO: 3 with substantially reduced affinity.

Claim 38 (withdrawn) The antagonist of claim 37 wherein the antagonist inhibits angiogenesis.

Claim 39 (withdrawn) The antagonist of claim 37 wherein the antagonist inhibits tumor growth.

Claim 40 (withdrawn) The antagonist of claim 37 wherein the antagonist is a polypeptide.

Claim 41 (withdrawn) The polypeptide of claim 40 wherein the polypeptide is a protein.

Claim 42 (withdrawn) The polypeptide of claim 40 wherein the polypeptide comprises SEQUENCE ID NO: 1.

Claim 43 (withdrawn) The polypeptide of claim 40 wherein the polypeptide is a monoclonal antibody.

Claim 44 (withdrawn) The polypeptide of claim 43 wherein the monoclonal antibody is FM 155.

Claim 45 (withdrawn) An antagonist that disrupts the localization of MMP-9 on a cell surface or blood vessel.

Claim 46 (withdrawn) The antagonist of claim 45 wherein the antagonist inhibits angiogenesis.

Claim 47 (withdrawn) The antagonist of claim 45 wherein the antagonist inhibits tumor growth.

Claim 48 (withdrawn) The antagonist of claim 45 wherein the antagonist is a polypeptide.

Claim 49 (withdrawn) The polypeptide of claim 48 wherein the polypeptide is a protein.

Claim 50 (withdrawn) The polypeptide of claim 48 wherein the polypeptide comprises SEQUENCE ID NO:1.

Claim 51 (withdrawn) The polypeptide of claim 48 wherein the polypeptide is a monoclonal antibody.

Claim 52 (withdrawn) The polypeptide of claim 51 wherein the monoclonal antibody is FM 155.

Claim 53 (withdrawn) A method of inhibiting angiogenesis in a tissue comprising administering the antagonist of claim 1.

Claim 54 (withdrawn) The method of claim 53 wherein said antagonist is administered intravenously, transdermally, intrasynovially, intramuscularly, intratumorally, intraocularly, intranasally, intrathecally, topically or orally.

Claim 55 (withdrawn) The method of claim 53 wherein said antagonist is administered in conjunction with chemotherapy.

Claim 56 (withdrawn) The method of claim 53 wherein said antagonist is administered in conjunction with radiation.

Claim 57 (withdrawn) The method of claim 53 wherein the tissue is inflamed and angiogenesis is occurring.

Claim 58 (withdrawn) The method of claim 57 wherein the tissue is present in a mammal.

Claim 59 (withdrawn) The method of claim 58 wherein the tissue is arthritic, ocular, retinal or a hemangioma.

Claim 60 (withdrawn) A method of inhibiting tumor growth or metastasis in a tissue comprising administering the antagonist of claim 1.

Claim 61 (withdrawn) The method of claim 60 wherein said antagonist is administered intravenously, transdermally, intrasynovially, intramuscularly, intratumorally, intraocularly, intranasally, topically or orally.

Claim 62 (withdrawn) The method of claim 60 wherein said antagonist is administered in conjunction with chemotherapy.

Claim 63 (withdrawn) The method of claim 60 wherein said antagonist is administered in conjunction with radiation.

Claim 64 (withdrawn) The method of claim 60 wherein the tumor or metastasis is a melanoma, carcinoma, sarcoma, fibrosarcoma, glioma or astrocytoma.

Claim 65 (withdrawn) A method of inhibiting psoriasis, macular degeneration, or restenosis in a tissue by administering the antagonist of claim 1.

Claim 66 (withdrawn) The method of claim 65 wherein said antagonist is administered intravenously, transdermally, intrasynovially, intramuscularly, intratumorally, intraocularly, intranasally, intrathecally, topically or orally.

Claim 67 (withdrawn) The method of claim 65 wherein administering the antagonist is in conjunction with chemotherapy.

Claim 68 (withdrawn) The method of claim 65 wherein administering the antagonist is in conjunction with radiation.

Claim 69 (withdrawn) A method of detecting angiogenesis in a tissue by contacting the antagonist of claim 1 with said tissue.

Claim 70 (withdrawn) The method of claim 69 wherein said tissue is *ex vivo*.

Claim 71 (withdrawn) The method of claim 69 wherein said tissue is *in vivo* and said antagonist is administered intravenously, transdermally, intrasynovially, intramuscularly, intratumorally, intraocularly, intranasally, intrathecally, topically or orally.

Claim 72 (withdrawn) The method of claim 69 wherein said antagonist is conjugated to a fluorochrome, radioactive tag, paramagnetic heavy metal, diagnostic dye or enzyme.

Claim 73 (withdrawn) A method of detecting tumors or tumor invasion in a tissue by administering the antagonist of claim 1.

Claim 74 (withdrawn) The method of claim 73 wherein said tissue is *ex vivo*.

Claim 75 (withdrawn) The method of claim 73 wherein said tissue is *in vivo* and said antagonist is administered intravenously, transdermally, intrasynovially, intramuscularly, intratumorally, intraocularly, intranasally, intrathecally, topically or orally.

Claim 76 (withdrawn) The method of claim 73 wherein said antagonist is conjugated to a fluorochrome, radioactive tag, paramagnetic heavy metal or diagnostic dye.

Claim 77 (withdrawn) A method for screening for MMP-9 antagonists comprising:

- a) providing a putative antagonist;
- b) measuring said putative antagonist's first affinity for binding with MMP-9;
- c) measuring a second affinity of SEQUENCE ID NO: 3 for binding with MMP-9;
- d) selecting said putative antagonist as an MMP-9 antagonist if said second affinity is substantially less than said first affinity.

Claim 78 (withdrawn) The method of claim 77 wherein said putative antagonist is a non-peptidic compound.

Claim 79 (withdrawn) The method of claim 77 wherein said non-peptidic compound is a small organic compound.

Claim 80 (withdrawn) The method of claim 78 wherein said non-peptidic compound is an oligonucleotide.

Claim 81 (withdrawn) The method of claim 77 wherein said putative antagonist is a polypeptide, a linear peptide or a cyclic peptide.

Claim 82 (withdrawn) The method of claim 77 wherein said putative antagonist is an antibody.

Claim 83 (withdrawn) The method of claim 82 wherein said antibody is monoclonal.

Claim 84 (withdrawn) The method of claim 82 wherein said antibody is polyclonal.

Claim 85 (withdrawn) The method of claim 77 wherein said first and said second affinities are measured by an enzyme linked immunosorbent assay.

Claim 86 (withdrawn) The method of claim 77 wherein second affinity is about 3 times less than said first affinity.

Claim 87 (withdrawn) The method of claim 77 wherein said second affinity is about 5 times less than said first affinity.

Claim 88 (withdrawn) The method of claim 77 wherein said second affinity is about 10 times less than said first affinity.

Claim 89 (withdrawn) A method for screening for $\beta 1$ integrin antagonists comprising:

- a) providing a putative antagonist;
- b) measuring said putative antagonist's first affinity for binding with a $\beta 1$ integrin;
- c) measuring a second affinity of SEQUENCE ID NO: 3 for binding with said $\beta 1$ integrin;

d) selecting said putative antagonist as a $\beta 1$ integrin antagonist if said second affinity is substantially less than said first affinity.

Claim 90 (withdrawn) The method of claim 89 wherein said putative antagonist is a non-peptidic compound.

Claim 91 (withdrawn) The method of claim 89 wherein said non-peptidic compound is a small organic compound.

Claim 92 (withdrawn) The method of claim 90 wherein said non-peptidic compound is an oligonucleotide.

Claim 93 (withdrawn) The method of claim 89 wherein said putative antagonist is a polypeptide, a linear peptide or a cyclic peptide.

Claim 94 (withdrawn) The method of claim 89 wherein said putative antagonist is an antibody.

Claim 95 (withdrawn) The method of claim 93 wherein said antibody is monoclonal.

Claim 96 (withdrawn) The method of claim 93 wherein said antibody is polyclonal.

Claim 97 (withdrawn) The method of claim 89 wherein said first and said second affinities are measured by an enzyme linked immunosorbent assay.

Claim 98 (withdrawn) The method of claim 89 wherein said second affinity is about 3 times less than said first affinity.

Claim 99 (withdrawn) The method of claim 89 wherein said second affinity is about 5 times less than said first affinity.

Claim 100 (withdrawn) The method of claim 89 wherein said second affinity is about 10 times less than said first affinity.

Claim 101 (withdrawn) A peptide comprising a sequence encoding an epitope recognized by an antagonist of claim 1.

Claim 102 (withdrawn) The peptide of claim 101 wherein said antagonist is a monoclonal antibody.

Claim 103 (withdrawn) The peptide of claim 102 wherein said antibody is FM 155.

Claim 104 (withdrawn) The peptide of claim 101 wherein said peptide is SEQ ID NO: 1.

Claim 105 (new) The antagonist of claim 1, wherein the proteolytic enzyme is a matrix metalloproteinase (MMP).

Claim 106 (new) The antagonist of claim 105, wherein the MMP is selected from a group consisting of MMP-1, MMP-2, MMP-3, MMP-7, MMP-9, and PUMP-1.